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After the abstract, please insert the paper copy of the Sequence Listing (on 7 sheets) submitted herewith.

REMARKS

The specification has been amended to incorporate the paper copy of the sequence listing pursuant to 37 C.F.R. § 1.821(c). A marked up version of the replacement paragraphs of the specification showing the amendments made is attached as Exhibit A, and a clean version of the replacement paragraphs of the specification is attached as Exhibit B.

The specification has amended to incorporate sequence identifiers pursuant to § 1.821(d). Applicants submit that the above-made amendments are fully supported in the instant application as originally filed, and do not constitute new matter. Applicants respectfully request that the above-made amendments be entered into the file history of the instant application.

CONCLUSION

Applicant respectfully requests entry of the foregoing amendments and remarks into the file history of the above-identified application.

Date October 5, 2001

Respectfully submitted,

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Enclosures

EXHIBIT A: MARKED UP VERSION OF THE SPECIFICATION

(U.S. APPLICATION NO. 09/489,873; ATTORNEY DOCKET NO. 9142-006-999)

On page 67, please amend the paragraph beginning “While antisense”, as follows:

While antisense nucleotides complementary to the Ob or ObR coding region sequence could be used, those complementary to the transcribed untranslated region are most preferred. For example, antisense oligonucleotides to the ObR coding region having the following sequences can be utilized in accordance with the invention:

- a) 5'-CATCTTACTTCAGAGAA-3' (SEQ ID NO: 1)
- b) 5'-CATCTTACTTCAGAGAAGTACAC-3' (SEQ ID NO: 2)
- c) 5'-CATCTTACTTCAGAGAAGTACACCCATAA-3' (SEQ ID NO: 3)
- d) 5'-CATCTTACTTCAGAGAAGTACACCCATAATCCTCT-3' (SEQ ID NO: 4)
- e) 5'-AATCATCTTACTTCAGAGAAGTACACCCATAATCC-3' (SEQ ID NO: 5)
- f) 5'-CTTACTTCAGAGAAGTACACCCATAATCC-3' (SEQ ID NO: 6)
- g) 5'-TCAGAGAAGTACACCCATAATCC-3' (SEQ ID NO: 7)
- h) 5'-AAGTACACCCATAATCC-3' (SEQ ID NO: 8)

On page 69, please amend the paragraph beginning “For example, hammerhead ribozymes”, as follows:

For example, hammerhead ribozymes directed to ObR mRNA having the following sequences can be utilized in accordance with the invention:

- a) 5'-ACAGAAUUUUUGACAAAUCAAAGCAGANNNUCUGAGNAGUCCUUAUUCAGAGAA-3' (SEQ ID NO: 9);
- b) 5'-GGCCCGGGCAGCCUGCCCAAAGCCGGNNNNCCGGAGNAGUCGCCAGACCGGCUCGUG-3' (SEQ ID NO: 10);
- c) 5'-UGGCAUGCAAGACAAAGCAGGNNNNCCUGAGNAGUCCUUAUUAUCCAAAGGAGUAA-3' (SEQ ID NO: 11);
- d) 5'-UAUAUGACAAAGCUGUNNNNACAGAGNAGUCCUUGUGUGGUAAAGACACG-3' (SEQ ID NO: 12);
- e) 5'-AGCACCAAUUGAAUUGAUGGCCAAAGCGGGNNNNCCCGAGNAGUCAACCGUAACAGUAUGU-3' (SEQ ID NO: 13);

f) 5'-UGAAAUUGUUUCAGGCUCCAAAGCCGGNNNNCCGGAGNAGUCAAGAAGAG
GACCACAUGUCACUGAUGC-3' (SEQ ID NO: 14);
g) 5'-GGUUUCUUCAGUGAAAUUACACAAAGCAGCNNNNGCUGAGNAGUCAGUUA
GGUCACACAUC-3' (SEQ ID NO: 15);
h) 5'-ACCCAUAUAACACAAAGCUGANNNNUCAGAGNAGUCAUCUGAAGGUUUC
UUC -3' (SEQ ID NO: 16).

On page 87, please amend the paragraph beginning "Expression of leptin", as follows:

Expression of leptin in osteoblasts could not be detected even after a long film exposure, indicating that an autocrine regulation was unlikely (Figure 5A). Leptin expression could also not be detected in whole bone samples, providing an indirect argument against a paracrine regulation of osteoblast function by leptin (Figure 5A). In any case, a paracrine and/or an endocrine regulation of osteoblast function by leptin would require that functional leptin receptors are present on osteoblasts. There are several transcripts of the leptin receptor, but only one, *Ob-Rb*, is thought to have signal transduction ability (Tartaglia *et al.*, 1995, Cell 83, 1263-1271; Chen *et al.*, 1996, Cell 84, 491-495; Lee *et al.*, 1996, Nature 379, 632-635). The expression of this transcript of leptin receptor is highly, although not strictly, hypothalamus-specific. RT-PCR experiments were performed to search for *Ob-Rb* transcripts in primary osteoblasts and whole bone samples. RT-PCR analysis (27 cycles) of *Ob-Rb* expression was performed on random-primed cDNAs using the following primers: 5'-TGGATAAACC CTTGCTCTTCA-3' (SEQ ID NO: 17), and 5'-ACACTGTTAATTTACACCAGAG-3' (SEQ ID NO: 18) (Friedman and Halaas, 1998, Nature 395, 763-770). Amplification of Hprt was used as an internal control for cDNA quality using the following primers: 5'-GTTGAGAGATCATCTCCACC-3' (SEQ ID NO: 19), and 5'-AGCGATGATGAACCAGGTTA-3' (SEQ ID NO: 20).

EXHIBIT B: REPLACEMENT PARAGRAPHS OF THE SPECIFICATION

(U.S. APPLICATION NO. 09/489,873; ATTORNEY DOCKET NO. 9142-006-999)

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- e) 5'-AATCATCTTACTTCAGAGAAGTACACCCATAATCC-3' (SEQ ID NO: 5)
- f) 5'-CTTACTTCAGAGAAGTACACCCATAATCC-3' (SEQ ID NO: 6)
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